

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau



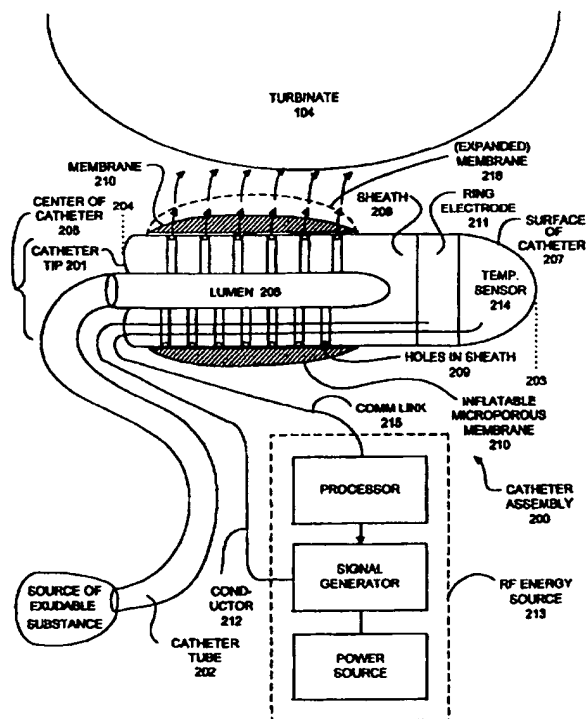
INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : A61B 17/39		A1	(11) International Publication Number: WO 97/43970
		(43) International Publication Date: 27 November 1997 (27.11.97)	
(21) International Application Number: PCT/US97/02960 (22) International Filing Date: 28 February 1997 (28.02.97) (30) Priority Data: 08/651,796 22 May 1996 (22.05.96) US (71) Applicant (for all designated States except US): SOMNUS MEDICAL TECHNOLOGIES, INC. [US/US]; 995 Benicia Avenue, Sunnyvale, CA 94086 (US). (71)(72) Applicant and Inventor: EDWARDS, Stuart, D. [US/US]; 658 Westridge Drive, Portola Valley, CA 94028 (US). (74) Agent: DAVIS, Paul; Wilson Sonsini Goodrich & Rosati, 650 Page Mill Road, Palo Alto, CA 94304-1050 (US).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.	

(54) Title: APPARATUS AND METHODS FOR ABLATING TURBINATES

(57) Abstract

The invention provides apparatus and a method for ablating at least a portion of an anterior part of the inferior nasal concha (turbinate). A catheter having a porous membrane coupled to a source of an exudable substance is disposed near the turbinate, whereby the exudable substance is emitted from the catheter and contacts the turbinate. An electrode is disposed near the turbinate, whereby the exudable substance aids the electrode in delivering ablating energy to the turbinate. The exudable substance is preferably a dielectric substance, such as saline, which aids in delivery of energy, and may include substances with other bioactive, chemoactive, or radioactive effects. The energy delivered to the turbinate is preferably RF energy which ablates the turbinate by heat and cell destruction. The catheter is preferably coupled to an energy source which provides energy delivered to the turbinate. The catheter preferably includes at least one sensor, such as a temperature sensor, and a communication link coupling the sensor to apparatus which controls the energy source, whereby feedback from the sensor is used to control operation of the energy source. The catheter may include a lumen which delivers the exudable substance to the porous membrane. The porous membrane may be microporous, or may include holes which allow the exudable substance to flow out from the catheter.



FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

APPARATUS AND METHODS FOR ABLATING TURBINATES

Cross Reference to Related Applications

This application is a continuation-in-part of the following co-pending applications: Application Serial No. 08/265,459, "Thin Layer Ablation Apparatus", filed June 24, 1994, in the name of Stuart D. Edwards; Each of
5 these applications is hereby incorporated by reference as if fully set forth herein.

BACKGROUND OF THE INVENTION

Field of the Invention

10 This invention relates to apparatus and methods for ablating turbinates.

Description of Related Art

In certain known medical conditions, the nasal structures (such as turbinates) can become enlarged, causing air space through the nasal passages to become restricted. In these cases it would be desirable to reduce the size of the
15 turbinates and thus alleviate the constriction of the nasal passages.

Known methods of reducing the size of the turbinates include surgery and pharmaceutical treatment. However, while these known methods achieve the goal of reducing the size of turbinates, they are subject to several drawbacks. Surgery has the drawback that it is complex, difficult, expensive, and sometimes
20 subjects the patient to risk which is disproportionate to the adverse medical condition. Pharmaceuticals have the drawback that they are sometimes not completely efficacious or efficient, and that they sometimes have adverse side effects. It sometimes happens that a patient is not a good candidate for surgery and is unable to achieve relief from pharmaceutical treatment.

25 Another known method for reducing the size of body structures is ablation. Known methods of ablation include use of chemical or laser ablation, or the use of mechanical devices such as rotatable blades, and using radiated RF energy. While known methods of chemical, laser, mechanical, or radiated RF energy ablation could achieve the goal of reducing the size of the patient's
30 turbinates, these known methods have the drawback that they are difficult to

control and could therefore cause indiscriminate ablation of turbinates.

Indiscriminate ablation of turbinates can cause loss of the proper function of that body structure. Since known methods of ablation have been unable to avoid substantial unnecessary loss of proper function of the patient's turbinates, these known methods have heretofore been inapplicable to turbinates.

5 Accordingly, it would be advantageous to provide improved apparatus and methods for ablation of turbinates.

SUMMARY OF THE INVENTION

10 The invention provides apparatus and a method for ablating at least a portion of a turbinate. A catheter having a porous membrane coupled to a source of an exudable substance is disposed proximate to the turbinate, whereby the exudable substance is emitted from the catheter and contacts the turbinate. In a preferred embodiment, an electrode is disposed proximate to the turbinate, whereby the exudable substance aids the electrode in delivering ablating energy to the turbinate.

15 The exudable substance is preferably a dielectric substance, such as saline, which aids in delivery of energy, and may include substances with other bioactive, chemoactive, or radioactive effects.

20 The energy delivered to the turbinate is preferably RF energy which ablates the turbinate by heat and cell destruction. The catheter is preferably coupled to an energy source which provides energy delivered to the turbinate. The catheter preferably includes at least one sensor, such as a temperature sensor, and a communication link coupling the sensor to apparatus which controls the energy source, whereby feedback from the sensor is used to control operation of the energy source.

25 The catheter may include a lumen which delivers the exudable substance to the porous membrane. The porous membrane may be microporous, or may include holes which allow the exudable substance to flow out from the catheter.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows a cut-away cross section of a patient's nose, showing a nasal cavity and a set of turbinates.

Figure 2 shows apparatus for ablating turbinates.

DESCRIPTION OF THE PREFERRED EMBODIMENT

Figure 1 shows a cut-away cross section of a patient's nose, showing a nasal cavity and a set of turbinates.

In a preferred embodiment, the patient is a mature adult human being. In alternative embodiments, the patient may be a child, a neonate, a fetus in utero.

In further alternative embodiments, the patient may be an animal subject to veterinary medicine.

A patient's nose 100 comprises at least one nasal cavity 101; the nasal cavity 101 comprises a set of turbinates 102, including a middle nasal concha (turbinate) 103 and an inferior nasal concha (turbinate) 104.

The inferior nasal concha (turbinate) 104 comprises an anterior portion 105 and a posterior portion 106.

Ablating the inferior nasal concha (turbinate) 104, and preferably ablating the anterior portion 105, does not substantially degrade the function of the inferior nasal concha 104. Ablating the inferior nasal concha (turbinate) 104, and preferably the anterior portion 105, can therefore be performed to achieve the goals of ablating the turbinates 102 without substantial suffering of disadvantages of ablating the turbinates 102.

Accordingly, a method embodying the present invention is to ablate the turbinates 102, but to limit that ablation to the inferior nasal concha 104, and preferably to limit that ablation to the anterior portion 105 thereof.

In a preferred embodiment, the anterior portion 105 is defined as being no larger than about one-third the volume of the inferior nasal concha 104. Thus, in a method embodying the present invention, when the anterior portion 105 is ablated, no more than about one-third of the inferior nasal concha 104 is ablated.

Apparatus for Ablating Turbinates

Figure 2 shows apparatus for ablating turbinates.

A catheter assembly 200 comprises a catheter tip 201 and a catheter tube 202. The catheter tip 201 comprises an structure having a distal end 203, a proximal end 204, a center 205 having a lumen 206, and a surface 207.

5 In a preferred embodiment, the catheter tip 201 has a straight elongated shape. In alternative embodiments, the catheter tip 201 may have another shape, such as a curved shape, or a shape adapted to fit into or to avoid a body structure, such as a curved shape disposed to fit inside a blood vessel or an eyelid. In a preferred embodiment, the catheter tip 201 is manufactured with a
10 predetermined (straight) shape. In alternative embodiments, the catheter tip 201 may be bendable or otherwise malleable to adopt a selected shape, may be dynamically adaptable to shapes selected by an operator, or may be actively adaptive to take on new shapes as it encounters obstructions or other body structures.

15 The center 205 of the catheter tip 201 is coupled to the catheter tube 202 at the proximal end 204 of the catheter tip 201, so that substances can flow from the catheter tube 202 into the lumen 206.

 In a preferred embodiment, the substance flowed from the catheter tube 202 into the lumen 206 comprises saline, the saline comprising distilled water
20 with a NaCl content of less than about 10% by weight. In alternative embodiments, the flowed substance may comprise saline with another amount of salt or another salt, may comprise a solution of other substances in other water or other solvents, or may comprise a substance with bioactive, chemoactive, or radioactive effects, such as an ablative acidic or alkaline substance, an antibiotic,
25 a compound used for chemotherapy, or a fluorescent or radioactive dye or marker, or some combination of these substances with each other or with some other substance.

 The surface 207 of the catheter tip 201 comprises a sheath 208. The sheath 208 has a generally cylindrical shape, thus surrounding the lumen 206,

and comprises a plurality of holes 209 disposed so that substances can flow from the lumen 206 out through the sheath 208 to outside the catheter tip 201.

In a preferred embodiment, the sheath 208 comprises a relatively inert and relatively hard substance, such as metallic copper or metallic silver. In alternative embodiments, the sheath 208 may comprise other relatively inert and relatively hard substances, such as gold, stainless steel, titanium, various plastic compounds, or some combination of these substances with each other or with some other substance.

In a preferred embodiment, the sheath 208 has a traverse diameter of about 6 french. One french is about 0.015 inches; thus 6 french is about 0.090 inches. In alternative embodiments, the sheath 208 may have another size, such as less than 2 french, between about 2 to about 6 french, or more than 6 french. In a preferred embodiment, the sheath 208 has a thickness of about 0.001 inches; this embodiment is particularly preferred in the case when the sheath 208 is copper.

The surface 207 of the catheter tip 201 also comprises a porous membrane 210 surrounding the sheath 208, disposed so that when substances flow out from the lumen 206, they encounter the membrane 210 and are trapped therein. As the membrane 210 is porous, the substances flow out through the membrane 210 and into proximity with the turbinate (specifically, the anterior portion 105 of the inferior nasal concha 104).

In a preferred embodiment, the membrane 210 comprises a microporous and inflatable balloon. As the substances flow into the membrane 210, pressure from the flow causes the balloon to inflate and to come into contact with the turbinate's anterior portion 105.

In a first preferred embodiment, the catheter tip 201 comprises at least one ring electrode 211 disposed proximate to the membrane 210. There may be a plurality of ring electrodes 211, disposed for example parallel with a first ring electrode 211 shown in figure 2 with their axes aligned with a long axis of the

catheter tip 201. The ring electrode 211 is coupled to a conductor 212 for coupling to an RF energy source 213.

In a second preferred embodiment, a surface (preferably an outside surface) of the membrane 210 is disposed with a plurality of electrodes. An example of a suitable surface for disposition on the membrane is shown in
5 Application Serial No. 08/319,373, "Thin Layer Ablation Apparatus", filed October 6, 1994, in the name of inventors James Baker, et al., and hereby incorporated by reference as if fully set forth herein. The surface is coupled to a conductor 212 for coupling to an RF energy source 213.

In alternative embodiments, the catheter tip 201 may comprise a
10 combination of the first and second preferred embodiment disclosed hereinabove may be used, such as a surface coupled using a conductor to a ring electrode 211, which is itself coupled to a conductor 212 for coupling to an RF energy source 213.

RF energy is supplied by an RF energy source 213. In a preferred
15 embodiment, the RF energy source 213 comprises a power source (or a power regulator coupled to a standard power source such as a wall socket or battery), a signal generator (such as a generator for pulses, sine waves, square waves, or some combination of these wave forms with each other or with some other wave form), and a processor for controlling the signal generator.

20 In a preferred embodiment, the signal generator generates pulses of RF energy having an RF radiation frequency between about 300 megahertz and about 700 megahertz, such as preferably about 465 megahertz. In alternative embodiments, the RF energy may have an RF radiation frequency in the microwave range or in another range of the electromagnetic spectrum.

25 The processor controls the signal generator to generate pulses to provide an effective amount of RF energy so as to deliver between about 5 and about 30 watts of RF energy to the turbinate's anterior portion 105, so as to raise a temperature of at least a part of the turbinate's anterior portion 105 to a temperature between about 40 degrees Celsius and about 120 degrees Celsius,
30 preferably above about 90 degrees Celsius.

In a preferred embodiment, the exudable substance, preferably saline, acts as an electrode or an electrolyte for delivering RF energy to the turbinate's anterior portion 105.

5 The catheter tip 201 comprises at least one temperature sensor 214, such as a thermocouple or thermistor. The temperature sensor 214 is coupled to a communication link 215 (such as a conductor), which is coupled to the processor. For example, in the case where the temperature sensor 214 comprises a thermocouple, the communication link 215 may comprise a D/A converter coupled to a register disposed for reading by the processor. The processor reads an sensor value from the sensor and, responsive thereto, controls the signal
10 generator so as to achieve delivery of an effective amount of RF energy to the turbinate's anterior portion 105. The processor thus uses the signal generator, catheter tip 201, ring electrode 211, and temperature sensor 214 as a feedback loop for controlled delivery of RF energy to the turbinate's anterior portion 105. For example, the processor may control the delivery of RF energy to achieve
15 delivery of a selected amount of energy, to achieve a selected temperature, or to achieve a selected amount of ablation of the turbinate's anterior portion 105.

In alternative embodiments, the catheter tip 201 may comprise other sensors, in addition to or instead of the temperature sensor 214, such as a chemical or biochemical sensor to detect ablation.

20

CLAIMS

1. Ablation apparatus, comprising
a source of an exudable substance;
a porous membrane coupled to said source;
means for disposing said porous membrane proximate to a turbinate;
5 and an electrode disposed proximate to the turbinate.
2. Apparatus as in claim 1, said means for disposing is positioned so
that said exudable substance is emitted from the catheter and contacts said
turbinate.
10
3. Apparatus as in claim 1, wherein said electrode is disposed a
distance from said turbinate to deliver an effective amount of energy to ablate at
least a portion of said turbinate.
4. Apparatus as in claim 3, wherein said energy comprises RF
15 energy having an RF radiation frequency between about 300 megahertz and
about 700 megahertz.
5. Apparatus as in claim 3, wherein said energy comprises
20 microwaves.
6. Apparatus as in claim 1, comprising
a conductor coupled to said electrode;
a signal generator coupled to said conductor and coupled to a power
25 source; and
a processor coupled to and disposed for controlling said signal generator.
7. Apparatus as in claim 6, wherein said processor is disposed for
controlling said signal generator to generate pulses to provide an effective

amount of RF energy so as to deliver between about 5 and about 30 watts of RF energy to at least a portion of said turbine.

8. Apparatus as in claim 6, wherein said processor is disposed for controlling said signal generator to generate pulses to provide an effective
5 amount of RF energy so as to raise a temperature of at least a portion of said turbine to a temperature above about 40 degrees Celsius.

9. Apparatus as in claim 6, comprising at least one sensor disposed proximate to said turbine and coupled to said processor.
10

10. Apparatus as in claim 9, wherein said sensor is disposed proximate to said means for disposing.

11. Apparatus as in claim 9, wherein said sensor is disposed
15 proximate to said electrode.

12. Apparatus as in claim 9, wherein said sensor comprises a temperature sensor.

20 13. Apparatus as in claim 1, wherein said porous membrane comprises an inflatable element.

14. Apparatus as in claim 1, wherein said porous membrane comprises a microporous element.
25

15. Apparatus as in claim 1,
wherein said source of an exudable substance comprises a lumen;
wherein said porous membrane comprises a sheath substantially
surrounding said lumen on a plurality of sides, said sheath defining a plurality of
30 passages through which said exudable substance may flow; and

wherein said porous membrane comprises an inflatable microporous element substantially surrounding said sheath on a plurality of sides.

5 16. Apparatus as in claim 1, wherein said means for disposing and said electrode are disposed so that said exudable substance provides substantial aid to said electrode in delivering energy to said turbine.

 17. Apparatus as in claim 1, wherein said exudable substance comprises saline.

10 18. Apparatus as in claim 1, wherein said exudable substance comprises a substance which aids in delivery of energy.

 19. Apparatus as in claim 1, wherein said exudable substance comprises a substance with a bioactive, chemoactive, or radioactive effect.

15 20. Apparatus as in claim 1, wherein said exudable substance comprises an ablative substance.

 21. Apparatus as in claim 1, wherein said exudable substance comprises an antibiotic.

 22. Apparatus as in claim 1, wherein said exudable substance comprises a dye or marker.

25 23. A method for ablation, said method comprising the steps of exuding a substance through a porous membrane into a region proximate to a turbine; and delivering an amount of RF energy effective to ablate said turbine.

24. A method as in claim 23, wherein said region contacts said turbine.

25. A method as in claim 23, wherein said RF energy has an RF radiation frequency between about 300 megahertz and about 700 megahertz.

5

26. A method as in claim 23, wherein said RF energy comprises microwaves.

27. A method as in claim 23, wherein said amount of RF energy is effective to deliver between about 5 and about 30 watts of RF energy to at least a portion of said turbine.

10

28. Apparatus as in claim 6, wherein said processor is disposed for controlling said signal generator to generate pulses to provide an effective amount of RF energy so as to raise a temperature of at least a portion of said turbine to a temperature above about 40 degrees Celsius.

15

29. A method as in claim 23, wherein said exudable substance provides substantial aid to said electrode in delivering energy to said turbine.

20

30. A method as in claim 23, wherein said exudable substance comprises saline.

31. A method as in claim 23, wherein said exudable substance comprises a substance with a bioactive, chemoactive, or radioactive effect.

25

32. A method as in claim 23, wherein said exudable substance comprises an ablative substance.

33. A method as in claim 23, wherein said exudable substance comprises an antibiotic.

34. A method as in claim 23, wherein said exudable substance comprises a dye or marker.

5

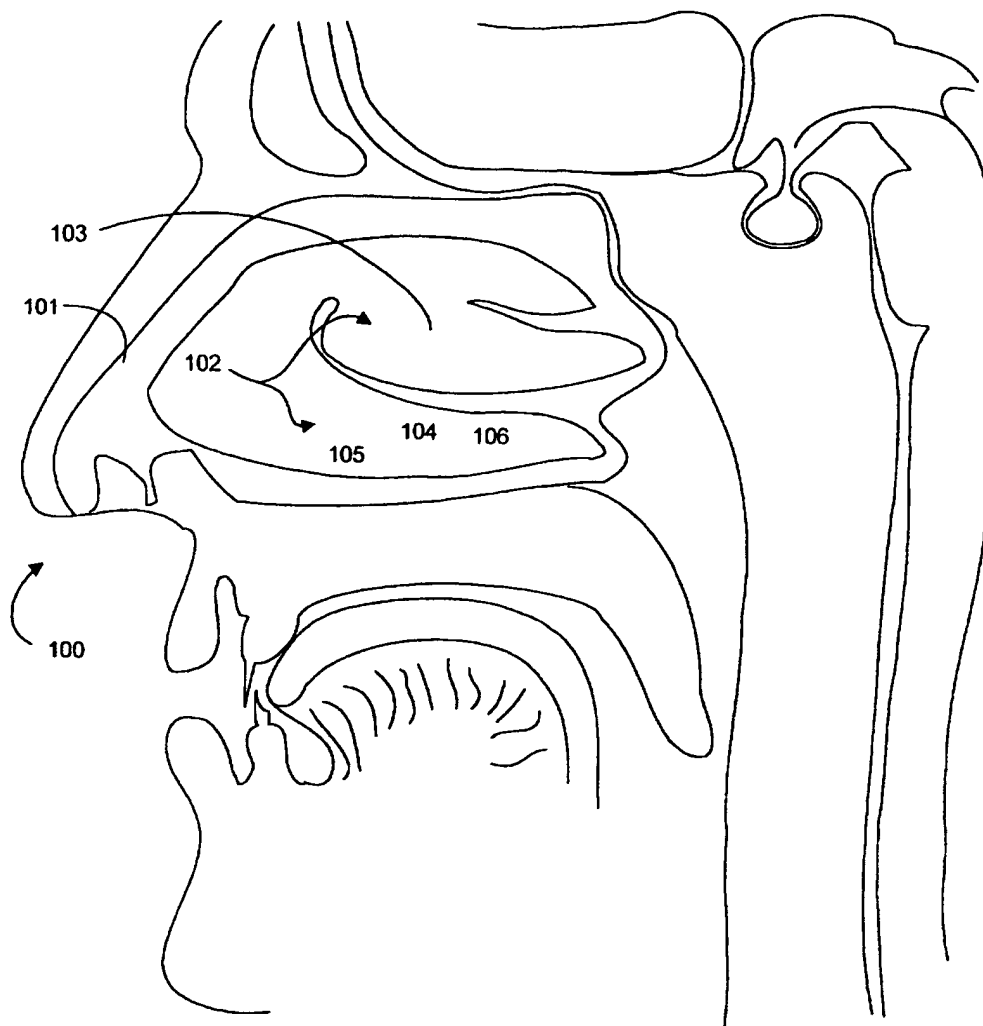


FIG. 1

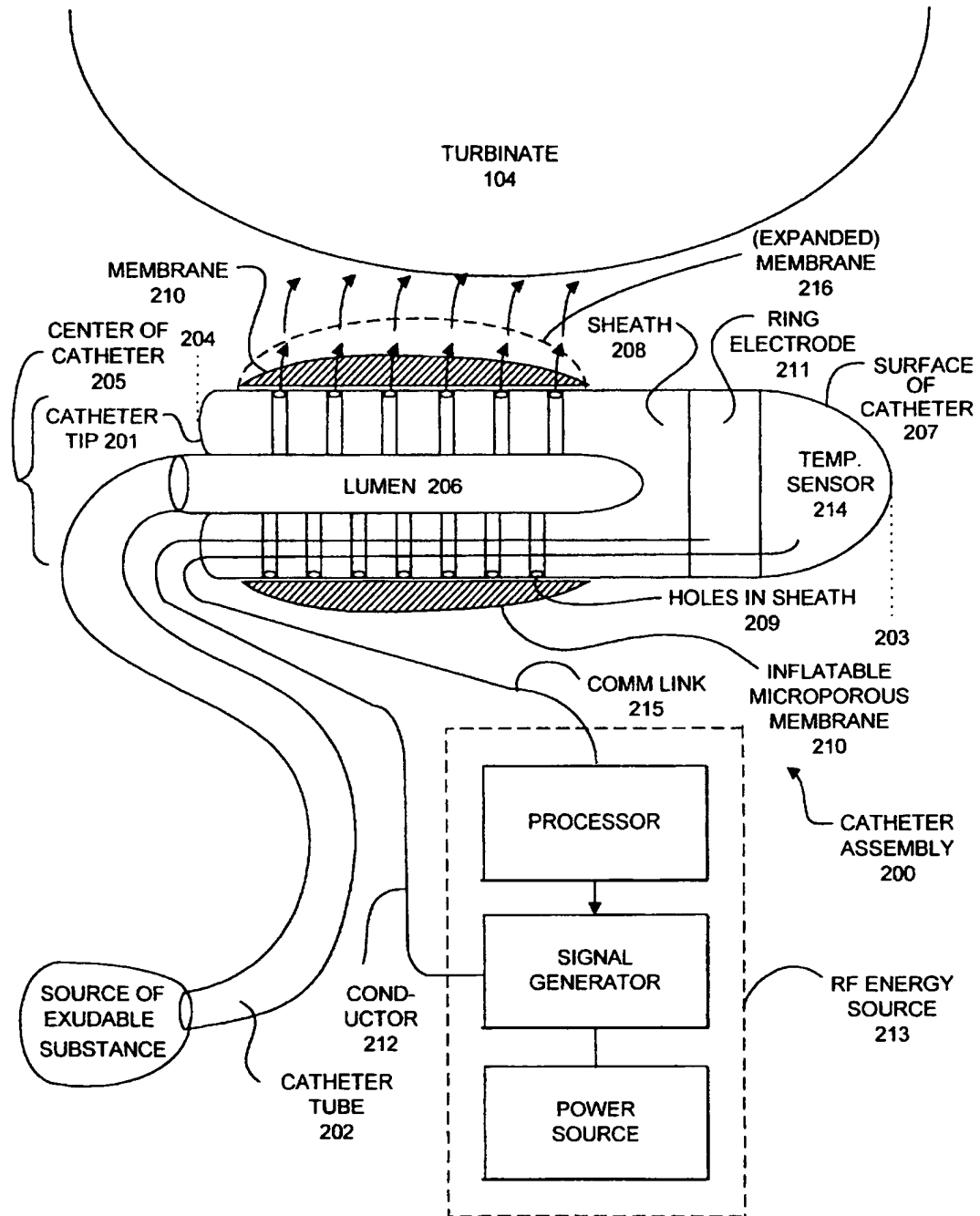


FIG. 2

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 97/02960

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61B17/39

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
Y	WO 96 00042 A (VIDACARE) 4 January 1996 see the whole document ---	1-6,9-18
Y	WO 95 31142 A (APPLIED MEDICAL RESOURCES) 23 November 1995 see abstract; figure 8 ---	1-6, 9-14, 16-18
Y	EP 0 392 837 A (GEDDES ET AL) 17 October 1990 ref. sign 108 see abstract; figure 1 ---	15
A	US 5 458 597 A (EDWARDS) 17 October 1995 see abstract; figure 1 ---	19-21
A	WO 95 25472 A (VIDAMED) 28 September 1995 -----	

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

22 October 1997

Date of making of the international search report

29. 10.97

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Papone, F

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 97/02960

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 23-34
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Internat / Application No

PCT/US 97/02960

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9600042 A	04-01-96	US 5505730 A	09-04-96
		US 5569241 A	29-10-96
		US 5558672 A	24-09-96
		AU 2871795 A	19-01-96
		AU 2998195 A	19-01-96
		CA 2193964 A	04-01-96
		EP 0767629 A	16-04-97
		NL 1000670 C	22-04-96
		NL 1000670 A	27-12-95
		WO 9600041 A	04-01-96
		US 5575788 A	19-11-96
WO 9531142 A	23-11-95	EP 0760628 A	12-03-97
EP 392837 A	17-10-90	US 4979948 A	25-12-90
		AT 133553 T	15-02-96
		DE 69025083 D	14-03-96
US 5458597 A	17-10-95	AU 1051495 A	29-05-95
		WO 9513113 A	18-05-95
		US 5472441 A	05-12-95
		US 5536267 A	16-07-96
		US 5507743 A	16-04-96
		US 5599345 A	04-02-97
		US 5599346 A	04-02-97
WO 9525472 A	28-09-95	US 5484400 A	16-01-96
		US 5542916 A	06-08-96
		AU 2196595 A	09-10-95